

REMARKS

Applicants appreciate the thorough examination of the present application as evidenced by the final Office Action dated June 19, 2006 (hereinafter, the "Final Action"). Claims 1-3 and 5-13 are pending in the present application, and Applicants respectfully submit that these claims are patentable in view of the claims amendments and remarks presented herein. Applicants respectfully request that should there be any issues preventing the allowance of the application upon the Examiner's consideration of the present Amendment, Applicants respectfully request that the Examiner contact the Applicants' representative noted below in order to discuss the outstanding issues.

I. Objections

The Office Action indicates that the specification is objected to because "the chapter "Gene Cloning, Transformation and Integration in *B. Licheniformis* DB104" on page 5 refers to *B. subtilis* DB104, transformed with vectors listed in Table 2," and "Applicants suggest that *B. subtilis* was transformed to contain the plasmid extrachromosomally and not integrated." Office Action, page 2. The Office Action further indicates that Claim 1 is objected to because enzymes are collected from the medium, but isolated therefrom. In response, Applicants have amended the specification as noted above, and Applicants have amended Claim 1 to recite the language suggested by the Examiner. Accordingly, Applicants respectfully submit that the objections to the specification and the objection to Claim 1 have been addressed, and Applicants respectfully request that such objections be withdrawn.

II. Claim Rejections Under 35 U.S.C. §112, Second Paragraph

Claim 2 stands rejected under 35 U.S.C. §112, second paragraph, on the basis that Claim 2 is confusing in recitation of the word "substrate." Office Action, page 3. Applicants have amended Claim 2 to recite "keratinase protein source."

Claim 3 stands rejected under 35 U.S.C. §112, second paragraph, and the Office Action indicates that a qualitative and quantitative description of "soy" is proper. *See* Office Action, page 4. Claim 3 has been amended to recite "soy flour."

Claim 11 stands rejected under 35 U.S.C. §112, second paragraph, on the basis that the claim language is unclear. *See* Office Action, page 4. Applicants have amended Claim 11 to delete the recitation "recombinant."

At least in view of the foregoing, Applicants respectfully submit that the rejections to the specification under 35 U.S.C. §112, second paragraph, have been addressed, and Applicants respectfully request that the rejection of Claims 2, 3 and 11 be withdrawn.

III. Claim Rejections Under 35 U.S.C. §112, First Paragraph, Written Description

Claims 1-13 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement: *See* Office Action, page 4. More specifically, the Office Action states the following:

The claims are directed to a large and variable genus of methods of using of integrants of *Bacillus* species having at least one heterologous *kerA* gene inserted into their chromosome. The claims are directed to the use of a large genus of transformants comprising one or several copies of any heterologous *kerA* gene. Applicants however disclose only *Bacillus subtilis* species having integrated to its chromosome the *kerA* gene of *Bacillus licheniformis* Disclosing this one recombinant *Bacillus* species transformed with only one identified *kerA* gene does not provide sufficient identifying characteristics of the genus of *Bacillus* species having one or multiple copies of any *kerA* gene integrated into their chromosome.

Office Action, page 5 (citations omitted).

Applicants have amended Claim 1 to recite that the recombinant *Bacillus* is one "selected from the group consisting of *Bacillus licheniformis* and *Bacillus subtilis* and having at least one heterologous *kerA* gene inserted into the chromosome thereof." Applicants respectfully submit that one skilled in the art would appreciate that Applicants were in possession of a recombinant *Bacillus* as recited in amended Claim 1.

The Office Action further indicates that Claim 6 is rejected because "Applicants fail to teach *kerA* gene of *Bacillus subtilis*. This is a complete lack of written description." Office Action, page 5. Applicants specifically state in the specification that "the *kerA* coding segment may be a *Bacillus licheniformis* or *Bacillus subtilis kerA* coding segment." Present Application, page 2, third full paragraph (emphasis added). Moreover, the specification states that "the *kerA* gene has been cloned and expressed from *B. subtilis*." Present Application, page 3, seventh full paragraph. Accordingly, Applicants respectfully submit that the specification teaches that the *kerA* coding segment may be a *Bacillus subtilis kerA* coding segment.

Claim 11 stands rejected on the basis that Claim 11 "imposes limitation on the genus of hosts to be used by the method to only those that are protease-deficient *Bacilli*." Office Action, page 5. As noted above, Applicants have amended Claim 11 to recite "a keratinase-deficient *Bacillus*."

Accordingly, at least in view of the foregoing, Applicants respectfully submit that the claim rejections under 35 U.S.C. §112, first paragraph, as lacking written description, have been addressed, and Applicants respectfully request withdrawal of this rejection.

IV. Claim Rejections Under 35 U.S.C. §112, First Paragraph, Enablement

Claims 1-13 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. See Office Action, page 6. More specifically, the Office Action summarizes the enablement rejection by stating, "without a guidance regarding the structure/origin of *kerA* gene, and the name/structure of *Bacillus* protease to be deficient in the host cells the experimentation left to the skilled artisan is improperly extensive and undue." Office Action, page 8.

As noted above, Applicants have amended Claim 1 to recite that the recombinant *Bacillus* is one "selected from the group consisting of *Bacillus licheniformis* and *Bacillus subtilis* and having at least one heterologous *kerA* gene inserted into the chromosome thereof," and Claim 11 has been amended to recite "a keratinase-deficient *Bacillus*." Applicants acknowledge that the touchstone for enablement is whether one reasonably skilled in the art could make and use the invention from the disclosures in the patent application coupled with information known in the art without undue experimentation. See Manual of Patent Examining Procedure §2164.01 (citing *In re Wands*, 858 F.2d 731, 737). Applicants respectfully submit that one of ordinary skill in the art could make and/or use the recombinant *Bacillus* according to the methods recited in the amended claims without undue experimentation.

Accordingly, at least in view of the foregoing, Applicants respectfully submit that the claim rejections under 35 U.S.C. §112, first paragraph, as lacking enablement, have been addressed, and Applicants respectfully request withdrawal of this rejection.

V. Claim Rejections Under 35 U.S.C. §103

Claims 1, 4, 6, 7, 9 and 10 stand rejected under 35 U.S.C. §103 as being obvious over Lin et al. Nucleotide Sequence and Expression of *kerA*, the Gene Encoding a Keratinolytic Protease of *Bacillus licheniformis* PWD-1, Applied and Environmental Microbiology 61: 1469-1474 (1995) (hereinafter, "Lin et al.") in view of van der Laan et al. Cloning, Characterization and Multiple Chromosomal Integration of a *Bacillus* Alkaline Protease Gene, Applied and Environmental Microbiology 57: 901-909 (1991) (hereinafter, "van der Laan et al."). See Office Action, page 8. The Office Action specifically states the following:

It would have been obvious for one having ordinary skills in the art to have *kerA* gene of Lin et al. and express it by integration to a chromosome of *B. subtilis* as van der Laan et al. did, using a commercially available integration plasmid pLAT8. The motivation would be to obtain a cell stably engineered to produce large quantities of keratinase. The motivation is taught by Lin et al., who point out that keratinase is an enzyme degrading feather from poultry waste. Thus, the enzyme is of importance for industrial and environmental reasons. The expectation of success is high, because van der Laan proved the successful production of serine protease by integrants of *Bacillus*.

Office Action, pages 9-10.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, the cited reference or combination of references must teach or suggest all the claim recitations. See *In re Wilson*, 165 U.S.P.Q. 494 (C.C.P.A. 1970) (emphasis added). Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in order to arrive at the claimed invention. See *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Third, there must be a reasonable expectation of success. See M.P.E.P. § 2143. Moreover, the law is clear with respect to obviousness. It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher." *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

Applicants respectfully submit that the combination of the cited references fails to teach or suggest all the recitations of the pending claims. As noted in the Office Action, "Lin

et al. do not teach the production of said keratinase in integrants of *Bacillus*." Office Action, page 9. van der Laan et al. does not supply the missing recitations as this reference is directed to the cloning, characterization and multiple chromosomal integration of a *Bacillus* **alkaline protease gene**. Accordingly, the combination of the cited references fails to teach or suggest a method of making a keratinase including culturing a recombinant *Bacillus* selected from the group consisting of *Bacillus licheniformis* and *Bacillus subtilis* and having at least one heterologous *kerA* coding sequence inserted into the chromosome thereof. Furthermore, the combination of the cited references also fails to teach or suggest a method of making a keratinase wherein the recombinant *Bacillus* produces **greater** quantities of keratinase than a corresponding wild-type *Bacillus* that does not have said at least one heterologous *kerA* coding sequence inserted into the genome thereof. Both Lin et al. and van der Laan, to the extent either of these reference discuss keratinase, are **silent** with respect to the **quantity** of keratinase produced. Thus, the cited references fail to teach or suggest all the recitations of the pending claims.

Applicants further submit that the requisite motivation to combine the cited references is lacking. The Office Action states that the "motivation" is taught by Lin et al. noting that keratinase is an enzyme that degrades feather from poultry waste, and thus, the enzyme is important for industrial and environmental reasons. See Office Action, page 10. Applicants respectfully submit, however, that the motivation to combine these references is clearly derived from the Applicants' specification. In fact, the Office Action refers to the Applicants' specification and states that "they [Applicants] used a modified protoplast method of Laan et al. for the integration of *kerA* gene into *Bacillus*. Office Action, page 9.

Thus, it is **only** through impermissible hindsight combined with picking and choosing portions of the cited references to the **exclusion** of deficient teachings, as discussed above, is one of ordinary skill in the art able to arrive at the present invention recited in Claim 1. For at least these reasons, Applicants respectfully submit that Claim 1 is not obvious in view of the combination of Lin et al. and van der Laan et al., and Claims 4, 6, 7 and 9-13, which are dependent therefrom, are also non-obvious in view of the cited references.

Accordingly, at least in view of the foregoing, Applicants respectfully submit that the claim rejections under 35 U.S.C. §103 have been addressed, and Applicants respectfully request withdrawal of this rejection.

Attorney Docket No. 5051-653
In re: Jason C. H. Shih et al.
Application No.: 10/661,172
Filed: September 13, 2003
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Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request that all outstanding objections and rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,



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